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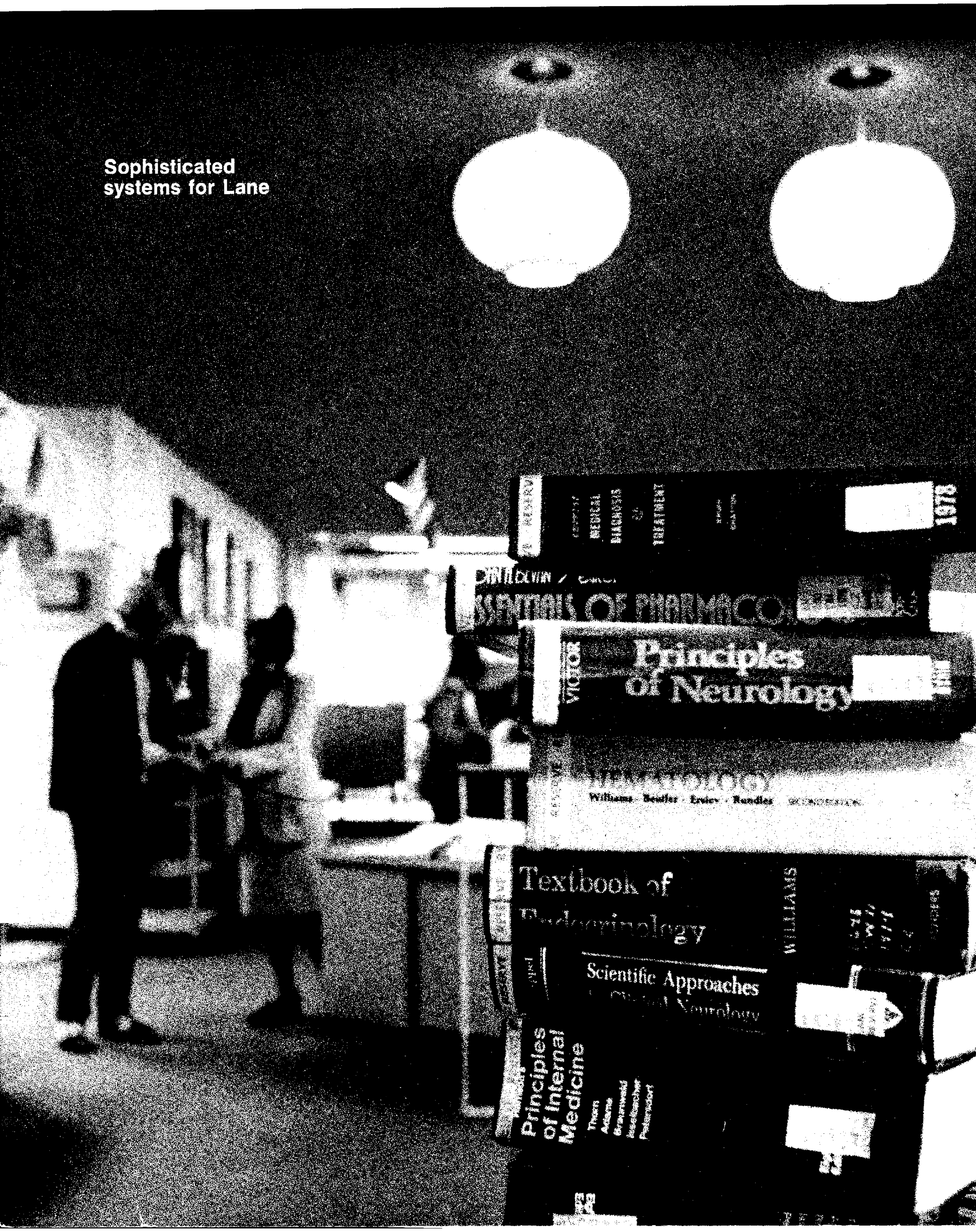
# Stanford MD

Sophisticated systems for Lane



# Joshua Lederberg: advocate of a 'new literacy'

## He has had enormous inpact on the University, catalyzing the interests of faculty in many fields.

by Bill Snyder

He is a Nobel laureate who wrote a widely syndicated science column for the *Washington Post*. He is an expert in computer systems who participated in negotiation of the biological weapons disarmament treaty. Joshua Lederberg embodies the successful juxtaposition of scientist and humanist, one who has balanced a brilliant scientific career in genetics with an active involvement in science policy.

This summer Lederberg, 53, left his post as chairman of the Department of Genetics at Stanford to become president of Rockefeller University in New York.

During his 20 years at Stanford, Lederberg pursued a variety of interests, from the intricacies of the cell to the enormities of space. Yet the hallmark of his career was an abiding commitment to communicate and to fulfill the needs of people. That commitment continues to underscore his contributions, as scientist and human being, and as the new administrator of a prestigious medical research institution.

The need to communicate is particularly important today with increasing public involvement in the conduct of science. Lederberg agrees that "social policy is too important to be left to the scientists," but he points out that in some areas this involvement has led to "irrational anxieties instead of open questioning. The public's fundamental suspicion of the scientist has gotten worse during the last few years," he says.

To a certain extent, this suspicion results from the nature of science itself. "Scientific information is provocative, but problematical. We don't have a well-integrated system for taking advantage of scientific development or for using that knowledge in the most effective way for policy decisions. Immense investments are being made in environmental health and protection, for instance, with very little understanding of the risks and benefits."

What is needed, he says, is a sector of scientifically trained analysts who are responsive to the needs of society. But that responsiveness must not be at the expense of creativity.

"Most scientfic work is awfully humdrum. While a lot of it has to be so, I thing we should operate more iconoclastically, and take larger gambles than we have in the past. I'd like to see more scientists putting their intellectual efforts into overturning old myths and opening new territories."

Encouraging responsiveness and creativity among scientists are not new concerns for Lederberg. Throughout his career he has pursued the answers to biological problems with a rugged pioneer spirit and an unflagging dedication to the betterment of mankind.

He sees his primary contribution as the research which earned him the Nobel prize in 1958, and membership in the National Academy of Sciences a year earlier.

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With the late Edward L. Tatum at Yale University in the late 1940s, Lederberg discovered that bacteria recombined, or mixed, their genes during reproduction. Later, at the University of Wisconsin, he and Norton Zinder, now at Rockefeller University, uncovered genetic transduction, the process by which genetic information carried by viruses is transmitted between organisms.

These discoveries paved the way for artificial manipulations in the laboratory using viruses, and later plasmids. The techniques he helped develop constitute the basis for present recombinant DNA research.

But Lederberg has never been satisfied to study genetics for its own sake. "The principal task of genetics," he said, "is scientific understanding, and the principal target for its application is the alleviation of individual distress."

Accordingly, after arriving at Stanford in 1959, he began to apply genetics to the study of diseases such as mental retardation. He participated in the President's Panel on Mental Retardation in 1961, and served as director of the Kennedy

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Laboratories for Molecular Medicine at Stanford, which conducted research into the genetics, development and neurobiology of retardation.

He became involved in a number of programs at Stanford, including the Human Biology Program for undergraduate students. "Lederberg has had enormous impact on the University, on people and on the projects he helped develop," says Dr. Eric Shooter, who joined the faculty in 1964, and now chairs the Department of Neurobiology. "He catalyzed my interest in neurobiology, just as he has catalyzed the interest of other faculty members in many different areas."

During the early 1960s, Lederberg also became involved in the nation's space program "to learn, for deep philosophical reasons, whether there was life outside the earth," he says. "That question led me to think about the definition of life. What are the fundamental criteria for detecting living systems, particularly if there are no holds barred with respect to history or environment?"

The probe to discover extraterrestrial life centered on Mars, a planet whose location in the solar system and mysterious canaled surface had intrigued astronomers for decades.

At first, Lederberg experimented with ways to detect micro-organisms in the Martian soil using a microscope and TV camera. That idea proved to be operationally unfeasible, so he developed mass spectrometry instruments which could detect miniscule amounts of complex organic molecules. The compounds are thought to be associated with the emergence of life forms on Earth.

Similar equipment was sent aboard the Viking spacecraft and reached Mars in 1976. The mission, which focused on the arid equatorial belt of the planet, failed to find any signs of life.

However, says Lederberg, that failure does not preclude the possibilities that life may exist on the polar caps, or that it existed in some previous time, but was wiped out in a climatic catastrophe. "Given the picture evidence of enormous river channels and yet the absence of fluid water on the planet surface at the present time, we have reason to think the latter hypothesis may be true," he says.

During the 1960s and early 1970s, Lederberg played an active role in forging national science policy. He served on the science information panel of the President's Science Advisory Committee. He was a member of the 1967 panel on medical and scientific ethics of the American College of Physicians.

Lederberg's concerns also brought him into the arena of the popular press. As a syndicated columnist for *The Washington Post* during the late 1960s, he discussed a variety of science topics, including developments in genetics, theories of intelligence, environmental pollution, and weapons proliferation.

During his involvement with the space program, Lederberg became schooled in organic chemistry and the use of computers for data analysis and problem solving activities. The capabilities of the newly developed "intelligent" computer programs, which employed a chain of reasoning analogous to human deduction, suggested a more general use in chemistry.

Lederberg joined forces with Edward Feigenbaum, chairman of the computer science department at Stanford, to explore this application. With the help of computer science professor Bruce Buchanan and chemistry professor Carl Djerassi, they constructed a program which generates structures of organic molecules from mass spectrometry data and an extensive knowledge base about how molecules exist in nature.

The program, called DENDRAL, is being used increasingly by chemists to check their structure proofs. In fact, a recent survey uncovered flaws in 25 percent of proofs published in scientific journals when they were checked by DENDRAL. A third of these errors were significant enough to warrant reexamination of the proofs.

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The success with DENTRAL stimulated the development of other prorams, such as MOLGEN, which aids in experiment design and data analysis in molecular genetics, and MYCIN, a computerized consultant in infectious diseases.

The increased load on computer resources made it necessary to seek larger facilities. In 1974, the National Institutes of Health supported the establishment of a national shared computer facility at Stanford for research in the medical applications of artificial intelligence. SUMEX (Stanford University Medical Experimental Computer) provides the hardware for 15 research projects conducted by scientists nationwide, and is continually increasing its community of users.

Feigenbaum, who took over this year from Lederberg as principal investigator of the program, credits his colleague for its success. "SUMEX as a national institution could not have occurred except for the truly brilliant and innovative leadership of Dr. Lederberg," he says. "He is a miracle worker."

One incidental, but important spinoff of computer networks such as SUMEX is the development of electronic mailing. The computer terminal provides efficiency in communicating the written word that is more immediate than the mail and more accurate than the telephone, without its interruption and queuing problems.

Lederberg calls it the emergence of a "new literacy," and anticipates that the technology will be available to the general public within the next few years.

In a recent article on the subject, he wrote: "The claim of science to universal validity is supportable only by virtue of strenuous commitment to global communication. The canon of publication insists upon public awareness and criticism of avowedly new knowledge."

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